

INT#N ATIONAL SEARCH REPORT

International Application No

PCT/EP2004/O53604

<p>A. CLASSIFICATION OF SUBJECT MATTER</p> <p>C12N15/11 A61K31/7125 A61K31/04 A61K31/166 A61K31/52</p> <p>A61K31/7048 A61P35/00 C07K14/495 A61K38/18</p>		
<p>According to International Patent Classification (IPC) or to both national classification and IPC</p>		
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols)</p> <p>C12N A61K A61P</p>		
<p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p>		
<p>Electronic data base consulted during the international search (name of data base and, where practical, search terms used)</p> <p>EPO-Internal , WPI Data, PAJ , BIOSIS , EMBASE</p>		
<p>C DOCUMENTS CONSIDERED TO BE RELEVANT</p>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>ARTEAGA C L ET AL: "REVERSAL OF TAMOXIFEN RESISTANCE OF HUMAN BREAST CARCINOMAS IN VIVO BY NEUTRALIZING ANTIBODIES TO TRANSFORMING GROWTH FACTOR-BETA" JOURNAL OF THE NATIONAL CANCER INSTITUTE, vol . 91, no. 1, 6 January 1999 (1999-01-06), pages 46-53, XP00040473</p> <p>ISSN: 0027-8874</p>	1, 3, 7-9, 11-16
Y	<p>the whole document</p> <p>-----</p>	1-17
Y	<p>WO 94/25588 A (BIOGNOSTIK GES ; BOGDAHN ULRICH (DE); BRYSCH WOLFGANG (DE); SCHLINGENS) 10 November 1994 (1994-11-10) cited in the application</p> <p>the whole document</p> <p>-----</p> <p>-/--</p>	1-17
<p><input checked="" type="checkbox"/> Further documents are listed in the continuation of box C <input checked="" type="checkbox"/> Patent family members are listed in annex</p>		
<p>* Special categories of cited documents</p> <p>'A' document defining the general state of the art which is not considered to be of particular relevance</p> <p>'E' earlier document but published on or after the international filing date</p> <p>L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>'O' document referring to an oral disclosure, use, exhibition or other means</p> <p>'P' document published prior to the international filing date but later than the priority date claimed</p> <p>'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>'X' document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>'Y' document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>'&' document member of the same patent family</p>		
<p>Date of the actual completion of the international search</p> <p>3 August 2005</p>		<p>Date of mailing of the international search report</p> <p>30 P' 2005</p>
<p>Name and mailing address of the ISA</p> <p>European Patent Office P B 5818 Patentlaan 2</p> <p>NL 2280 HV Hilversum</p> <p>Tel (31-70) 340-2040, Tx 31 551 epo nl,</p> <p>Fax (31-70) 340 3016</p>		<p>Authorized officer</p> <p>Andres , S</p>

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/ 03604

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WOJTOWICZ-PRAGA SLAWOMIR: "Reversal of tumor-induced immunosuppression by TGF-beta inhibitors." INVESTIGATIONAL NEW DRUGS, vol. 21, no. 1, February 2003 (2003-02), pages 21-32, XPO08035079 ISSN: 0167-6997 cited in the application the whole document -----	1-17
A	YU D ET AL: "HYBRID OLIGONUCLEOTIDES: SYNTHESIS, BIOPHYSICAL PROPERTIES STABILITY STUDIES, AND BIOLOGICAL ACTIVITY" BIOORGANIC & MEDICINAL CHEMISTRY, vol. 4, no. 10, 1996, pages 1685-1692, XP000644792 ISSN: 0968-0896 -----	
A	RUBENSTEIN MARVIN ET AL: "Inhibition of PC-3 prostate cancer cell growth in vitro using both anti sense oligonucleotides and taxol." MEDICAL ONCOLOGY (TOTOWA), vol. 20, no. 1, 2003, pages 29-35, XPG08035083 ISSN: 1357-0560 the whole document -----	
A	WO 99/63975 A (BIOGNOSTIK GES ; BRYSCH WOLFGANG (DE); SCHLINGENSIEPEN KARL HERMANN (D) 16 December 1999 (1999-12-16) cited in the application -----	
A	WO 01/68146 A (BIOGNOSTIK GES ; SCHLINGENSIEPEN KARL HERMANN (DE); SCHLINGENSIEPEN RE) 20 September 2001 (2001-09-20) cited in the application -----	
P,X	WO 2004/005552 A (MONIA BRETT P ; DOBIE KENNETH W (US); FREIER SUSAN M (US); ISIS PHARMA) 15 January 2004 (2004-01-15) page 54 - page 55 page 79; example 5 page 91 - page 100; examples 15,16 -----	1-3,5-16

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2004/053604

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

- 1 ☒ Claims Nos 18-23, 25
because they relate to subject matter not required to be searched by this Authority, namely
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
- 2 ☒ Claims Nos : -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically
see FURTHER INFORMATION sheet PCT/ISA/210
- 3 **D** Claims Nos
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 34(a)

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows-

see additional sheet

- 1 ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims
- 2 ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee
- 3 ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos
- 4 ☒ No required additional search fees were timely paid by the applicant. Consequently this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos
1-23, 25 (all partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest

☐ No protest accompanied the payment of additional search fees

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-23,25 (all partially)

A composition associating a human TGF-beta1 anti sense oligonucleotide (SEQ IDs 1-21) with an antineoplastic chemotherapeutic agent, and its uses in the treatment of neoplasms.

2. claims : 1-23,25 (all partially)

As for subject 1., but concerning human TGF-beta2 anti sense oligonucleotides (SEQ IDs 22-48).

3. claims : 1-23,25 (all partially)

As for subject 1., but concerning human TGF-beta3 anti sense oligonucleotides (SEQ IDs 49-78).

4. claims : 4-13,15-17,19-23,25 (all partially)

As for subject 1., but concerning human PGE antisense oligonucleotides (SEQ IDs 79-89).

5. claims : 4-13,15-17,19-23,25 (all partially)

As for subject 1., but concerning human VEGF antisense oligonucleotides (SEQ IDs 90-126).

6. claims : 4-13,15-17,19-23,25 (all partially)

As for subject 1., but concerning human IL-10 antisense oligonucleotides (SEQ IDs 127-146).

7. claims: 26-29

Peptide fragments of TGF-beta1, -beta2 and/or -beta3, compositions comprising them and their use in the treatment of neoplasms.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 18-23,25

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: -

1. - The dependency of present claim 4 to claim 1 is not correct as far as concerning SEQ IDs 79-146. Indeed, claim 1 concerns TGF-beta antagonists, whereas said SEQ IDs are antisenses against other target genes (according to pages 31 to 34 of underlying application). For the purpose of the search, claim 4 has therefore be considered as independent.

2. - Present claims 1-3,7-23,25 relate to compositions associating (at least) two compounds defined solely by reference to a desirable characteristic or property, namely their ability to antagonise TGF-beta, stimulate the function of the immune system or immune cells, or to inhibit cell proliferation and/or induce cell death. The claims cover all associations of all compounds having these characteristics or properties, whereas the application provides support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC for only a very limited number of such combinations. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 84 EPC). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compositions associating TGF-beta1 antisense oligonucleotides (SEQ IDs 1-21 in claim 4) with chemotherapeutic agents.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

out during examination before the EPO (see EPO Guideline C-VI, 8.5),
should the problems which led to the Article 17(2) declaration be
overcome .

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/053604

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9425588	A	10-11-1994	AT 211762 T 15-01--2002
			AT 235549 T 15-04--2003
			AU 6794594 A 21-11--1994
			DE 69429617 D1 14-02--2002
			DE 69429617 T2 22-08--2002
			DE 69432375 D1 30-04--2003
			DE 69432375 T2 12-02--2004
			JP 3555952 B2 18-08--2004
			JP 8509370 T 08-10--1996
			JP 3600831 B2 15-12--2004
			JP 2004024264 A 29-01--2004
			US 6455689 B1 24-09--2002
WO 9963975	A	16-12-1999	AT 274923 T 15-09-2004
			AU 5154999 A 30-12-1999
			CA 2334960 A1 16-12-1999
			DE 69919869 D1 07-10-2004
			DE 69919869 T2 29-09-2005
			ES 2226414 T3 16-03-2005
			JP 2002517434 T 18-06-2002
WO 0168146	A	20-09-2001	AT 304858 T 15-10-2005
			AU 6010901 A 24-09-2001
			EP 1133988 A1 19-09-2001
			JP 2003526684 T 09-09-2003
			US 2003186906 A1 02-10-2003
WO 2004005552	A	15-01-2004	AU 2003281327 A1 23-01-2004
			US 2004006030 A1 08-01-2004